REMARKS

In a July 26, 2001 telephonic interview between Examiner Winkler and the undersigned, Examiner Winkler indicated that the papers filed on July 5, 2001 and June 29, 2001 by Nancy V. Connelly of Schering-Plough Corporation would not be entered into the record of the subject application until an Associate Power of Attorney was filed for Ms. Connelly. Examiner Winkler indicated that she would issue a written record (Interview Summary) indicating that the U.S. Patent and Trademark Office would not abandon the application. Furthermore, on September 7, 2001, during a telephone conference between Examiner Jim Housel and the undersigned, Examiner Housel indicated that he would accept papers, including an Amendment and an Associate Power of Attorney (which is attached hereto as Exhibit C), if such papers were filed by facsimile today, September 7, 2001. Accordingly, applicants understand that the subject application is pending today and that this Amendment and the accompanying Associate Power of Attorney are being timely filed.

STATUS OF CLAIMS

Claims 2, 6, 48-52, 55, 56, 62-64 and 83-85, 89 and 90 are pending and under examination. Claim 61 was withdrawn. Claims 6, 61 and 89 have been cancelled without prejudice. Claims 2, 56, and 90 have been amended.

No new matter has been added by virtue of these claim amendments.

The Applicants' acknowledge with thanks the Examiners' withdrawal of the following rejections in the Office Action mailed January 2, 2001: the rejection of claims

2, 87 and 88 under 35 U.S.C. §112, first paragraph; the rejection of claims 2, 55 and 86 under 35 U.S.C § 112, second paragraph; the rejection of claims 2, 46, 47 and 83 under 35 U.S.C. § 112, second paragraph; the rejection of claims 2, 87 and 88 under 35 U.S.C § 112, second paragraph; the rejection of claims 2, 55 and 86 under 35 U.S.C. § 112, second paragraph; the rejection of claims 2, 55 and 86-87 under 35 U.S.C. § 103(a).

Applicants attach an annotated version of the claims indicating amendments as Exhibit A.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

A. Rejection of Claims 2, 83, 89 and 90 under 35 U.S.C.§112, First Paragraph.

Claims 2, 83, 89 and 90 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. The Examiner stated at page 3 of the Office Action dateed January 2, 2001 that changing the wording to "an isolated nucleic acid consisting essentially of SEQ ID NO: 5" would obviate this rejection.

In response, while disagreeing with the Examiner's view, Applicants' have amended claims 2, and 90 and cancelled claim 89 in the interest of expediting prosecution. In accordance with the Examiner's suggestion, Applicants have amended claim 2 to replace the recitation of "wherein the isolated nucleic acid sequence is at least about 70% homologous with the nucleic acid sequence" with --consisting essentially of the nucleotide sequence of--. Applicants have amended claim 90 to replace the recitation of "comprising" with "consisting essentially of." Since claim 89 would be duplicative in scope of claim 2 as amended, claim 89 has been cancelled.

In support for this amendment, Applicants contend that the specification provides the cDNA encoding feline CD86. This was also pointed out by the Examiner on page 3 of the Office Action dated March 29, 2000. Support for this amendment can be found, for example, on page 45, lines 15-21 and in Example 1A on pages 37-41 of the scpecification. Applicants note that the cDNA comprises a whole open reading frame. The specific nucleotide sequence, SEQ ID NO: 5, of the full length open reading frame is disclosed by the Applicants. One of skill in the art would recognize from the disclosure that SEQ ID NO: 5 can be readily combined with additional nucleotide sequences. Applicants therefore believe the amendment of claims 2 and 90 obviates the rejection of claim 2, its dependent claim 83 and the independent claim 90. Reconsideration and withdrawal of this rejection is respectfully requested.

B. New Rejection of Claims 2, 6, 48-52, 55, 56, 62-64 and 85-85 Under 35 U.S.C. § 112, First Paragraph

Claims 2 and dependent claims 6, 48-52, 55, 56, 62, 63, 64 and 83-85 are rejected to under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Specifically, the Examiner states that "[t]he specification, while being enabling for SEQ ID NO: 5 coding for the polypeptide of SEQ ID NO: 6, does not reasonably provide enablement for the other homologous sequences or polynucleotide sequence comprising the SEQ ID NO: 5." (January 2, 2001 Office Action at pages 4-5.)

While disagreeing with the Examiner's view, Applicants have amended claim 2 in the interest of expediting prosecution. Specifically, as set forth above, "wherein the isolated nucleic acid sequence is at least about 70% homologous with the nucleic acid sequence" has been replaced with "consisting essentially of the nucleotide sequence of". Support for this amendment can be found, for example, on page 45, lines 15-21, Example 1A on pages 37-41 and Figure 3A.

In light of these amendments, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, first paragraph rejection of claims 2 and dependent claims 6, 83, 48-52, 55, 56, 62, 63, 64 and 83-85.

C. Rejections of Claim 56 Under 35 U.S.C. § 112, First Paragraph - Biological Deposit

The Examiner rejected Claim 56 under 35 U.S.C. § 112, first paragraph, stating that the specific plasmid vector claimed therein must be readily available or obtained by a

repeatable method set forth in the specification, or otherwise known and readily available to the public.

The Examiner noted that a deposit of the plasmid vector B7-2 #19-2/011298 (ATCC Accession No. 209821) was made. The Examiner stated that if a deposit is made under the terms of the Budapest Treaty, than an affidavit or declaration by Applicants, or statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

In reply, Applicants traverse the rejection and maintain that claim 35 is fully enabled by the specification. A deposit pursuant to the Budapest Treaty of the plasmid vector B7-2 #19-2/011298 (ATCC Accession No. 209821) was made on April 29, 1998 with the American Type Culture Collection, as stated in the specification. A copy of the Deposit Receipt is attached hereto as Exhibit B. All restrictions on the availability of this deposit will be irrevocably removed upon issuance of a patent from this application.

For clarity, the recitation of "plasmid" has been deleted from dependent claim 56 since the claim it depends from is drawn to "a vector." Thus, Applicants respectfully request that the Examiner reconsider and withdraw this rejection of claim 56.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 2 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner contends that the use of the term "about" renders this claim indefinite.

In response and as set forth above, Applicants believe that the amendment to claim 2 obviates this rejection since the recitation of "at least about 70% homologous" has been deleted from the claim. Reconsideration and withdrawal of this rejection is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 2 and dependent claims 6, 48-42 [sic; 52?], 55, 56, 62-64 and 83-85 are rejected to under 35 U.S.C. § 102 (b) as allegedly being anticipated by Freeman *et al.* (WO95/03408). As discussed below, Applicants traverse this rejection and contend that the pending claims are patentable over the above-cited reference.

The independent pending claims as amended are directed to (1) an isolated nucleic acid encoding a feline CD86 ligand or a soluble feline CD86 ligand consisting essentially of the nucleotide sequence of SEQ ID NO: 5; and (2) an isolated nucleic acid consisting essentially of a nucleotide sequence which encodes a feline CD86 ligand or a feline soluble CD86 ligand having the amino acid sequence shown in SEQ ID NO: 6.

Freeman *et al.* refer to the human B7-2 B lymphocyte antigen. It provides an isolated nucleic acid with a specific nucleotide sequence which encodes the human antigen. As the Examiner states on page 7-8 of the Office Action dated March 29, 2000, Freeman *et al.* do not specifically teach the nucleotide and corresponding amino acid sequence of feline CD86.

In support of the rejection, the Examiner alleges at page 7 of the January 2, 2001 Office Action that "Freeman *et al.* discloses the nucleotide sequence that is at least about 70% homologous to the instant sequence." In response and as set forth above, Applicants believe that the amendment to claim 2 obviates this rejection since the recitation of "at

least about 70% homologous" has been deleted from the claim. The nucleotide sequences in Freeman *et al.* do not encode a feline CD86 ligand or a soluble feline CD86 ligand. The nucleotide sequences and corresponding amino acid sequences provided in Freeman *et al.* are different from the nucleotide and corresponding amino acid sequences of Applicants' disclosure given as SEQ ID NO: 5 and SEQ ID NO: 6, respectively. It was noted by the Examiner on page 8 of the Office Action dated March 29, 2000 regarding Applicants' disclosure that "it appears that the specific sequence of SEQ ID: 5 and 6 are free of the prior art." Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim 2 is rejected to under 35 U.S.C. § 102 (b) as allegedly being anticipated by Azuma *et al.* (WO95/06738). As discussed below, Applicants traverse this rejection and contend that the pending claims as amended are patentable over the above-cited reference.

Azuma *et al.* describe a human B70 protein. Azuma *et al.* disclose the specific nucleotide sequence, SEQ ID NO: 1, of a human B70 protein and the corresponding amino acid sequence, SEQ ID NO: 2, of the human B70 protein. In support of this rejection, the Examiner states that "Azuma *et al.* disclose a nucleotide sequence SEQ ID NO: 1 that is at least about 70% homologous to the instant sequence."

Again, Applicants believe that the amendment to claim 2 obviates this rejection since the recitation of "at least about 70% homologous" has been deleted from the claim. The nucleotide sequences in Azuma *et al.* do not encode a feline CD86 ligand or a soluble feline CD86 ligand. The nucleotide sequences and corresponding amino acid sequences provided in Azuma *et al.* are not the same as the SEQ ID NO: 5 and SEQ ID

NO: 6 of the Applicants' disclosure. Reconsideration and withdrawal of this rejection is respectfully requested.

REJECTION UNDER 35 U.S.C. § 103 (a)

The Examiner has maintained the rejections of claims 2, 6, 46, 48-52, 55, 56, 62-64 and 83-85 stand rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Freeman *et al.* (U.S. Pat. No. 5,942,607). Applicants traverse this rejection and contend that the amended claims are patentable over Freeman *et al.*

Freeman *et al.* refer to the human B7-2 B lymphocyte antigen. They provide an isolated nucleic acid with a specific nucleotide sequence which encodes the human antigen. As the Examiner acknowledges on pages 7-8 of the Office Action dated March 29, 2000, Freeman *et al.* do not disclose the nucleotide and corresponding amino acid sequence of feline CD86.

Freeman *et al.* do not disclose or suggest the desirability of obtaining a feline homologue of CD86. Freeman *et al.* mention only human and murine systems, focusing on potential uses only of interest in human medicine. They state that in column 1, lines 62-66 that "The importance of the B7:CD28/CTLA4 costimulatory pathway has been demonstrated *in vitro* and in several *in vivo* model systems. Blockade of this costimulatory pathway results in the development of antigen specific tolerance in murine and human systems." Freeman *et al.* further note in column 4, lines 11-15, that "The methods of the invention may also be useful therapeutically, in the treatment of autoimmune diseases, transplantation rejection and established graft versus host disease in a subject." In contrast, the motivation of Applicants to fulfill a need in the art, as

discussed at page 1, lines 20-30 of the instant specification, is not provided by Freeman *et al.*:

> Currently there are no successful vaccines for the prevention of feline immunodeficiency disease and feline infectious peritonitis disease in cats. Current feline leukemia virus vaccines are available, but their level of efficacy remains in questionable and in some cases may cause the disease. Therefore, there is a need in the art for agents and compositions that provide protection from these and other diseases where there is not yet an existing vaccine or that improve the efficacy of existing and commonly used vaccines. In addition, vaccination of kittens is difficult due to the inability to overcome maternal antibodies in kittens. Safe and effective agents to help overcome these barriers are also needed.

In short, Freeman *et al.* do not provide a motivation for obtaining a feline homologue of CD86. Applicants were the first to recognize the desirability of obtaining CD86 and its potential to solve this need in the art.

The recitation from Freeman *et al.* at column 11, lines 56-62, that the Examiner cites for support of this rejection states:

> B lymphocyte antigens isolated for one species (e.g., humans) which exhibit cross-species reactivity may be used to modify T cell mediated immune response in a different species (e.g., mice). Isolation of cDNA clones from other species can also be accomplished using human cDNA inserts, such as B7-2 cDNA, as hybridization probes."

Applicants point out that Freeman *et al.* do not define the type of "cross-species reactivity" to which is referred. There is no mention or teaching of an assay or method that one could use to determine if this property exists in different species. Applicants point out that nowhere does the reference state that cross-species reactivity exists between human and feline B lymphocyte antigens. This would be a prerequisite to using this methodology since there is no teaching of an assay or method to measure this property. There is no direction given by Freeman *et al.* as to which portion of such a human cDNA insert to use as a hybridization probe. There is no direction or suggestion

to look in felines since the motivation given to perform such an isolation is based on species which exhibit "cross-species reactivity."

The Examiner further attempts to support the rejection by stating at page 7 of the Office Action dated March 29, 2000 that "CD28 is expressed on resting T-cells and is the receptor for CD86. Binding of CD86 to CD28 causes resting T-cells to proliferate and secret(e) IL-2." No citation was given for this reference. However, Applicants have reviewed the Freeman *et al.* reference for this statement and believe the following quotation found in Freeman *et al.* at column 1, lines 49-52, is the citation to which the Examiner refers:

> B7 is the counter-receptor for two ligands expressed on T-lymphocytes. The first ligand, termed CD28, is constitutively expressed on resting T cells and increases after activation. After signaling through the T cell receptor, ligation of CD28 induces T cells to proliferate and secrete IL-2. The second ligand, termed CTLA4 is highly homologous to CD28 but it is not expressed on resting T cells and appears to following T cell activation. Although B7 has a higher affinity for CTLA4 than for CD28, its function is still unknown.

In this citation, Freeman *et al.* states that the function of B7 is still unknown. This suggests that at the time investigators in this field of the art were open to the possibility that entities could be discovered which would ligate CD28 other than B7. Therefore, just isolating B7 alone may not provide the desired effect.

The Examiner goes on to cite a passage from Freeman *et al.* at Column 3, lines 36-38, which states that "...the use of nucleic acids of the invention, especially cDNAs, to enhance the immunogenicity of a mammalian cell. In preferred embodiments, the mammalian cell is a tumor cell..." as allegedly providing motivation to clone a CD28 ligand from felines. Applicants point out that Freeman *et al.* appear to be referring to the

use of nucleic acids that contain the nucleotide sequence of their own cDNA as set forth in SEQ ID NO: 1 of their disclosure. This is at best a motivation to make or use only the nucleic acids of their own invention. Freeman *et al.* disclose the cDNA for the human B7-2 B lymphocyte antigen. They provide an isolated nucleic acid with a specific nucleotide sequence that encodes the human antigen and the corresponding amino acid sequence of the human antigen. Freeman *et al.* do not disclose that a feline CD28 ligand exists let alone advocate the use of the nucleic acids encoding it.

In short, Applicants point out that Freeman *et al.* do not provide a motivation or an expectation of success for obtaining a feline homologue of CD86. Freeman *et al.* do not disclose that a feline CD28 ligand or a feline CD86 exists or is likely to exist.

It would not have been obvious to one of skill in the art to make or use the Applicants' disclosed nucleic acids for the reason that the nucleotide sequence for feline CD86 was unknown at the time.

Accordingly, reconsideration and withdrawal of the rejections of the pending claims under 35 U.S.C. § 103 is respectfully requested.

CONCLUSION

In view of the above amendments and discussion, reconsideration and withdrawal of these grounds for rejection, and allowance of pending claims 2, 48-52, 55, 56, 62-64, 83-85 and 90, are respectfully requested.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone her at the number provided below.

Respectfully submitted,

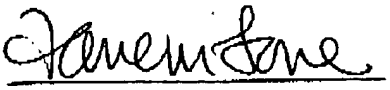

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EXHIBIT A - Version with Markings to Show Changes Made

2. (2x Amended) An isolated nucleic acid encoding a feline CD86 or a feline soluble CD86 ligand [wherein the isolated nucleic acid sequence is at least about 70% homologous with the nucleic acid sequence] consisting essentially of the nucleotide sequence of [shown in] SEQ ID NO: 5.

56. (Amended) The [plasmid] vector of claim 55 designated B7-2#19-2/011298 (ATCC Accession No. 209821).

90. (Amended) An isolated nucleic acid [comprising] consisting essentially of a nucleotide sequence which encodes a feline CD86 ligand or a feline soluble CD86 ligand having the amino acid sequence [shown in] of SEQ ID NO: 6.

ATCC

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BU[redacted]

THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Coôper & Dunham, LLP
Attn: John P. White, Esq.
1185 Avenue of the Americas
New York, NY 10036

Deposited on Behalf of: Schering-PloughAnimal Health (Ref. Docket 54957)

Identification Reference by Depositor:	**ATCC Designation**
Plasmid DNA containing feline B7-1 gene, PSI-B7-1 / 871-35	209817
Plasmid DNA containing feline B7-1 gene, 917-19.8/16	209818
Plasmid DNA containing feline CD28 gene, PSI-CD28 #7 / 100296	209819
Plasmid DNA containing feline CTLA-4 #1 / 091997	209820
Plasmid DNA containing feline B7-2, #19-2/011298	209821

The deposits were accompanied by: ___ a scientific description _ a proposed taxonomic description indicated above. The deposits were received April 29, 1998 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested June 10, 1998. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Barbara M. Hailey

Barbara M. Hailey, Administrat r, Patent Depository

Date: June 24, 1998

cc: Bob Alderson

BP/9